REMARKS

Consideration of this application is requested in view of the amendments to the claims and the remarks presented herein.

The claims in the application are claims 3 to 9, 11 to 13 and 18 to 30, all other claims having been cancelled.

The undersigned wishes to thank the Examiner in charge of the application and Jose Dees, her supervisor, for the courtesies extended to the undersigned and to Dr. Burtin the French patent attorney for the Applicants as well as Dr. J. Paris one of the inventors of the application and Sylvie Delpy who is in charge of the in-house patent department for the assignee at the interview granted on November 14, 2001. A copy of the interview summary report is submitted herewith since the Examiner did not have the application before her at the time of the interview.

In related application Serial No. 284,147 filed April 7, 1999, there was a rejection of the claims therein as being obvious over the Lanquetin et al patent No. 5,891,867 as well as the Fraser et al reference. The Examiner in the related application deemed that the invention was obvious from these references since in the Examiner's opinion, the same method of treatment was being claimed in both instances.

As pointed out in the amendment filed in the related application and the Sitank-Wares declaration filed herwith, the reference does not teach the claims of the present application which is directed to the prevention of estrogen deficiencies in menopausal women or preventing osteoporosis and cardiovascular disorders in said menopausal women by continuously administering without interruption to menopausal women in need thereof an amount of a mixture of 0.3 to 3 mg of an estrogen and 0.3 to 1.25 mg of nomegestrol or an ester thereof.

Applicants' process differs from the two references in the fact that the treatment in both references is sequential. In the Lanquetin et al patent, the treatment is for estrogen deficiencies and re-establishment of an endometrial cycle in menopausal women by administering orally to menopausal women in three different sequences an estrogen alone followed by an estrogen-progestin combination and then a placebo for the duration of the month. In contrast thereto, Applicants' method relates to the continuous administration without interruption of the estrogen and a specific progestin, namely, nomegestrol or an ester thereof in specific ranges. As can be seen from the graph submitted herewith concerning the Lanquetin et al patent, the Frazer paper and the present invention in the two prior art references cited by the Examiner in the related case dealing with a sequential treatment, there is an interruption of the sequential treatment wherein there is a bleeding similar to the normal menstrual cycle.

In contrast thereto, in Applicants' continuous without interruption method of administering both components together, there is no withdrawal bleeding and there is no normal menstrual cycle. This can be seen from the graph submitted herewith. Also submitted herewith is a table comparing the treatment. As can be seen from the table, the prior art are both related to sequential treatment v. Applicants' continuous treatment. In the prior art, the menstrual cycle was regular while there is no menstrual cycle whatsoever in Applicants' method. There is withdrawal bleeding in both instances of the prior art and no bleeding in Applicants' method. Moreover, with respect to the endometrium, the prior art is secretory while in Applicants' method, it is atrophic. Therefore, these references do not suggest Applicants' claimed invention.

As discussed with the Examiners at the interview, there is a reissue Patent No. 36,247 of Plunkett et al which contains claims, particularly claim 23, with a continuous method of administration of an estrogen and a progestin within certain specific ranges. Applicants will concede that this teaches the use of a progestin, but not Applicants'. In addition, Applicants progestin has perfect metabolic tolerance which is contrary to 19-nor testosterones and MPA, the progestins disclosed by Plunkett, and no deleterious effect on blood vessels contrary to MPA. Therefore, it is clear that the Plunkett et al patent does not anticipate or render obvious Applicants' method.

Copies of the Plunkett et al and Lanquetin et al and Fraser et al references are submitted herewith for the Examiner's convenience. The distinctions with respect to the Plunkett et al patent are further pointed out in this application, particularly on pages 5 through 10 of the application.

In addition, at the interview, there was discussed the differences between the present application and the earlier filed application Serial No. 284,147 which corresponds to the French patent No. 2,754,179 referred to on page 10 of the application. Basically, the difference between the earlier application and the present application is the fact that the present application uses lower doses of the known nomegestrol, namely, 1.25 mg or less. This lower dosage rate in the nomegestrol and its esters is characterized by very marked antimitotic and antiproliferative action as can be seen from the data on page 20, for instance.

As pointed out on page 22 of the application, the highest percentage of atrophic endometrium was found at the lowest progestative dose and this effect decreased as the nomegestrol acetate dose increased. These results are unexpected in the sense that they show that low doses of nomegestrol and its esters continuously administered with an estrogen are capable of preventing the growth of uterine mucosa and keep it in atrophic condition whereas at higher doses as taught in the companion application, they are insufficient to induce a secretory

transformation of the endometrium. This is a surprising decoupling of the antiestrogenic effect of nomegestrol and its esters from its progestational effect when continuously administered with estrogens. Therefore, there is a clear distinction between the two applications.

In view of the amendments to the claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
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Enclosures